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09/715,909	11/17/2000	Ronald D. Flannagan	35718/204664	5613

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ALSTON & BIRD LLP
PIONEER HI-BRED INTERNATIONAL, INC.
BANK OF AMERICA PLAZA
101 SOUTH TYRON STREET, SUITE 4000
CHARLOTTE, NC 28280-4000

EXAMINER
HAYES, ROBERT CLINTON

ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/715,909	Applicant(s) Flannagan et al
	Examiner Robert C. Hayes, Ph.D.	Art Unit 1647

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *May 10, 2002* .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-3, 7, 8, 10-18, and 26-36* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-3, 7, 8, 10-18, and 26-36* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *11,12*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Claim Rejections - 35 U.S.C. § 101

1. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 15-16 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. For example, the current recitation of " a cell" or "a transformed host cell" encompasses a human organism. It is suggested that amending the claims to "an isolated transformed host cell" should obviate this rejection.

Claim Rejections - 35 U.S.C. § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 7-8, 10-18 & 26-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No proper antecedent nor conception in context of that described in the specification at the time of filing Applicants' invention is apparent for the broader concept of any Bt toxin

binding protein, versus a "receptor" polypeptide that binds Bt toxin; thereby, constituting new matter.

3. Claims 1-3, 7-8, 10-18 & 26-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, for the reason made of record in Paper No: 10 and as follows.

The specification describes the sole *Ostrinia nubilalis* polypeptide of SEQ ID NO:2. No other *Ostrinia nubilalis* polypeptides are described. The specification also describes the *Heliothis Zea* polypeptide of SEQ ID NO:4 and the *Spodoptera frugiperda* polypeptide of SEQ ID NO:6, which are all from lepidopteran insects. No different polypeptides from any other species are described. In other words, no adequate written description of what constitutes any different species, allelic variant (i.e., as both encompassed by the recitation of "at least % identity), fragments or different generic heterologous polypeptides fused to random fragments of SEQ ID NO:2 is provided within the instant specification, or known in the art, which possess the recited activity. In addition, the specification fails to describe what critical amino acids define any distinguishable and assayable *Ostrinia nubilalis* polypeptide activity. Nor could one skilled in the art reasonably visualize what constitutes such generic heterologous proteins encompassed by these claims, as currently and broadly claimed.

In contrast to Applicants' assertions on pages 7-9, the current claims are not limited to a described genus with a "recitation of a representative number of cDNAs" or with a "recitation of structural features common to the members of the genus", which further currently includes claims merely including fragments of SEQ ID NO:1 where no open reading frame exists or encompass unknown and undescribed heterologous amino acid sequences fused to fragments, in general, where the critical amino acids necessary for Bt toxin activity are not recited, and otherwise, are unknown. Therefore, consistent with that stated on page 18 of the specification, "it is difficult to predict the exact effect of the substitution, deletion, or insertion in advance of doing so"; thereby, not meeting the written description requirements under 35 U.S.C. 112, first paragraph.

It is suggested that amending the claims to isolated nucleic acid molecules comprising a nucleotide sequence encoding a "lepidopteran insect receptor" polypeptide with the recited % identities and the recited functional activity of binding *"Bacillus thuringiensis* (Bt) toxin" may obviate this rejection.

Applicant is directed toward the Revised Interim Utility and Written Description Guidelines, Federal Register, Vol.64, No.244, pages 71427-71440, Tuesday December 21, 1999.

4. Claims 1-3, 7-8, 10-18 & 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the specific polypeptide depicted as SEQ ID NO:2, does not reasonably provide enablement for any biological functional equivalent polypeptides/

fragments with little structural characterization and no distinguishable recited functional characteristics. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims, for the reason made of record in Paper No: 10 and as follows.

In contrast to Applicants' assertions on pages 9-11 of the response, a fragment that does not consist of at least the extracellular part of this receptor would not reasonably bind Bt toxin (e.g., see pages 19 and 35 of the specification), and therefore, would prevent the skilled artisan from knowing how to make the invention as claimed, because the "Cry1A binding site is encoded by residues 4038-4547 of SEQ ID NO:1 (i.e., at least 510/3= 170 specific amino acid residues), and not encoded by 22 nucleotides that merely encode 7 random amino acid residues, which clearly would not constitute the extracellular domain of this receptor as described on page 19 of the specification; nor does such constitute a polypeptide of "approximately 210 and 205 kDa" as described on page 34 of the specification that putatively "binds CrylA(b)". In contrast, random deletions/truncations to the polypeptide of SEQ ID NO:2, as currently claimed, would alternatively result in an inactive encoded protein; consistent with the teachings of Skolnick and Fetrow previously made of record. Moreover, Rudinger states on page 3 that "it is impossible to attach a unique significance to any residue in a sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of the same sequence". Rudinger further states on page 6 that "the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must

be determined from case to case by painstaking experimental study". Therefore, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for any Bt toxin binding function would prevent the skilled artisan from determining whether any random mutation, modification or truncation to the specific amino acid sequence of SEQ ID NO: 2 could be made which retains the desired function of the instant invention, because any random mutation, truncation or modification, especially when fused to additional random heterologous amino acid sequences, would be predicted to adversely alter its biologically active 3-dimensional conformation, without requiring undue experimentation to determine otherwise.

Therefore, Applicants arguments are not persuasive for those claims currently encompassing fragments of SEQ ID NO:2.

5. Claims 1-3, 7-8 & 10-18 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Only hybridization to the "fully complementary strand" of a polynucleotide would possibly produce a Bt toxin polypeptide encoded from the sense strand; thereby, being indefinite (i.e., as it relates to claim 1).

6. Claims 7-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as

the invention, because it is ambiguous what metes and bounds constitute "at least one polypeptide *of interest*", in which use of this relative terms further defines nothing, and therefore, is indefinite.

7. Claims 1-3, 7-8, 10-18, 26-29 & 33-35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is ambiguous exactly what the recitation "at least about" entails, because "about" refers to a range of +/- 5%, whereas, the recitation "at least" removes the lower limit of the claimed range of "about 60/70/75/85/95%"; thereby, being contradictory.

Claim Rejections - 35 U.S.C. § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 7-8 & 10-16 are rejected under 35 U.S.C. 102(b) as being anticipated by Bulla et al. (U.S. Patent 5,693,491).

Bulla et al. teach a receptor for a Bt toxin (cryIa(b)) from *M. sexta* that is 63.9 % identical to SEQ ID NO:1 (i.e., as least about 60% identical; col. 2; as it relates to claim 1) and encodes a

polypeptide that is 60.7 % identical to SEQ ID NO:2 (i.e., as least about 52% and 60% identical; as it relates to claims 7 & 2-3). In that nucleotide residue #s 978-993, 1524-1544, 1555-1572, 2511-2530, etc. are 100% identical, the limitation of "hybridizes under stringent conditions to SEQ ID NO:1", etc. is inherently met (i.e., as it relates to claim 1(h), where "encoding a fusion protein"/Bulla's protein comprising... at least one polypeptide... encoding at least about 15 contiguous residues... set forth in SEQ ID NO:2 is also anticipated (i.e., residue #s 1023-1038 of SEQ ID NO:2; as it relates to claim 7(h)). In that Bulla et al. disclose expression cassettes/ vectors and transformed cells comprising this nucleic acid molecule, which include insect and mammalian cells, as well as microorganisms/procaryotic cells/*E. coli*, claims 7-8 & 10-16 are anticipated (i.e., cols. 4-5).

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (703) 305-3132. The examiner can normally be reached on Monday through Thursday, and alternate Fridays, from 8:30 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623. The fax phone number for this Group is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert C. Hayes, Ph.D.
October 1, 2002

GARY KUNZ
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600